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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 09/464,767 | 12/16/1999 | GERALD WAYNE BOTH | 50179-073 | 8030 |

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WASHINGTON, DC 20005-3096

EXAMINER

PRIEBE, SCOTT DAVID

| ART UNIT | PAPER NUMBER |
|----------|--------------|
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1632

DATE MAILED: 04/16/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

SM.

Office Action Summary**Application No.**

09/464,767

Applicant(s)

BOTH ET AL.

Examiner

Scott D. Priebe

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 17 & 18 Mar. & 6 Oct. 2003.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 25-29, 31-37 and 39-51 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☒ Claim(s) 28 and 48 is/are allowed.
- 6) ☒ Claim(s) 25-27, 29, 31-37, 39-47 and 49-51 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 06 October 2003 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☒ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☒ Certified copies of the priority documents have been received in Application No. 08/776,274.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

The amendment filed 17 Mar. 2003 and declaration filed 18 Mar. 2003 under 37 CFR 1.132 have been entered. A duplicate of these papers was filed 02 May 2003. The proposed replacement Fig. 13 has not been entered for the reasons set forth in the letter of 4 Sep. 2003. The substitute drawings filed 6 Oct. 2003 have been entered.

The terminal disclaimer filed on 17 March 2003 disclaiming the terminal portion of any patent granted on this application which would extend beyond the expiration date of US Pat. No. 6,020,172 has been reviewed and is accepted. The terminal disclaimer has been recorded.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Oath/Declaration

The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

The oath or declaration is defective because:
The specification to which the oath or declaration is directed has not been adequately identified. See MPEP § 601.01(a).

The application was filed 16 Dec. 1999 with a preliminary amendment and an unsigned declaration. Consequently, the preliminary amendment is part of the original disclosure and the specification as amended must be identified in the declaration. The executed declaration filed 10 Jul. 2002 identifies the application as being "amended by the Preliminary Amendment filed concurrently herewith." However, the preliminary amendment was filed concurrently with the

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specification, not with the declaration of 10 Jul. 2002. The declaration should identify the application as -- amended by the Preliminary Amendment filed concurrently therewith -- (therewith rather than herewith) or as -- amended by the Preliminary Amendment filed December 16, 1999 --.

Claim Objections

Claim 29 is objected to because of the following informalities:

Previously presented claim 29 recited "28457", whereas amended claim 29 recites "28487" in line 5. However, the marked-up copy of amended claim 29 does not indicate that the term was amended.

Also, claim 29 is needlessly verbose and redundant, and somewhat confusing (also see rejection under 35 USC 112, 2nd para. below). It is suggested that the claim be amended to read:

-- An isolated DNA molecule comprising a nucleotide sequence identical to nucleotides 1-29,574 of SEQ ID NO: 3 except for a deletion or alteration in nucleotides ... to ... or ... to ... of SEQ ID NO: 3-- (filling in the appropriate nucleotide numbers)

Appropriate correction is required.

Claim Rejections - 35 USC § 112

Claims 25, 26, 29, 31-37, 39-47, and 49-51 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably

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convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 25, 31, 41, 42, 45, 47 and 49 have been amended to delete the limitation requiring the DNA molecule/plasmid/vector to “encode a functional ovine adenovirus genome”. While this specific language was itself deemed to be new matter, it was at least consistent with the specification and original claim 1 in that an isolated DNA molecule that hybridized to the complement of SEQ ID NO: 3 would be an adenoviral genome. Claim 36 has been amended to limit the vector to an adenoviral vector. Original claim 1 recited that the DNA molecule would encode an ovine adenoviral genome either “substantially as shown in Fig. 1”, which is SEQ ID NO: 1 not SEQ ID NO: 3, or “a functionally equivalent nucleic acid sequence.” The preliminary amendment added subject matter at page 10, following line 15, that defined “substantially” as meaning hybridizing under high stringency conditions, and defined the range of conditions considered to be “high stringency”. The specification (pg. 6, lines 3-12) defined the limitation “functionally equivalent nucleic acid sequence” to mean either changes in nucleotide sequence relative to OAV287 (SEQ ID NO: 1) that altered viral polypeptide coding sequence but not the amino acid sequence encoded, or if the amino acid sequence encoded was changed, that the change would not substantially alter the biological activity of the viral polypeptide (the latter was held not to be enabled by the specification in the Office action of 3 July 2001).

Amended claims 25, 31, 36, 41, 42, 45, 47 and 49 (and their dependent claims) now require only that the (second) DNA molecule or second nucleotide sequence hybridize to nt. 1-29,574 under high stringency conditions. This limitation places no constraints on the function of the DNA molecule or second nucleotide sequence or to what extent it must correspond to all of

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nt. 1-29,574 of SEQ ID NO: 3. For example, a DNA molecule/plasmid or adenoviral vector that comprises 50 contiguous nucleotides of the OAV287 genome (and no more) would meet the limitation of these claims because it would hybridize to the complement of SEQ ID NO: 3 under the high stringency conditions disclosed in the specification. Page 3, line 32 to page 4, line 9 and original claims 4-7 is essentially the only description of DNA molecules would do not necessarily be able to function as an adenoviral genome comparable to OAV287 itself. These contemplated fragments of the genome are described as sharing at least one characteristic that they comprise at least 15 nucleotides of SEQ ID NO: 1 that is “substantially unique” to OAV287. With respect to claim 26 requiring that the DNA molecule be 90% identical to nt. 1-29,574 SEQ ID NO: 3, such a molecule might lack one or both ITRs, in addition to other types of changes relative to SEQ ID NO: 1. The specification does not describe DNA molecules of unspecified length and relationship to SEQ ID NO: 1 or 3 that hybridize to the complement of SEQ ID NO: 3. Consequently, there is no evidence that applicant had contemplated or was in possession of such embodiments when the application was filed. The specification generally describes DNA molecules (including plasmids and adenoviral vector genomes) that comprise an OAV287 genome or variant of the OAV287 genome that is substantially identical to the OAV287 genome, wherein the variant adenoviral genome comprises all *cis*- and *trans*-acting sequences required for viral replication and virion production in ovine cells. The claims should be amended to clearly limit the second “DNA molecule” or “second nucleotide sequence” to one that is itself capable of replicating autonomously as an adenovirus in sheep cells, in accordance with the original disclosure.

Claim 29 (and claims 50 and 51) has been amended by adding 30 nucleotides to all of the nucleotide positions recited in the previous claim 29. Applicant has provided no explanation for this change or indicated where the original specification supports the amendment, and it is not immediately apparent how it does.

Claims 33, 34, 36-37, 39-47 and 49 are directed to or require a plasmid or adenoviral vector which comprises: 1) first or second nucleotide sequence; and 2) a third nucleotide sequence. As the claims are written, the third nucleotide sequence must be outside of and separate from the adenoviral genome, i.e. the third sequence is not inserted into the adenoviral genome. For example, if the third sequence were inserted into the SEQ ID NO: 3, the resulting DNA would not be SEQ ID NO: 3 and the vector or plasmid would not comprise SEQ ID NO: 3. The specification discloses plasmids which contain an adenoviral genome and a marker gene as separate, adjacent parts, e.g. pOAV100, or contain an adenoviral genome wherein the bacterial vector is inserted into the adenoviral genome, e.g. pOAV287Cm. The first could meet the claim limitations, whereas the second cannot. The specification also describes a viral vector comprising a non-adenoviral sequence, encoding a polypeptide or RNA, inserted into an ovine adenoviral vector genome. However, this disclosed embodiment also is not embraced by the claims, since it would not comprise the recited first or second sequence. This part of the rejection would be overcome by amending claims 36, 41, 42, 45, 47 and to recite that the third nucleotide sequence is inserted into the first or second nucleotide sequence (second sequence inserted into the first sequence for claim 49) in a region not essential to replication of the adenoviral genome in ovine cells (see specification, pp. 18-20).

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Applicant is reminded that it their burden to indicate where support is to be found in the original specification for new claims and claim limitations. See MPEP 714.02 and 2163.06(I). A statement that merely alleges that the amendments “correct various typographical, correct dependencies and to expressly recite that which was implicit in the original claims” and generally summarizing what the original claims were directed to does not meet this burden. Applicant should explain how the new claims and claim limitations are directly supported by the original disclosure.

Claim 41 remains rejected under 35 U.S.C. 112, first paragraph, for the reasons of record set forth in the Office action of 16 Sep. 2002, because the specification, while being enabling for a method of delivering a DNA molecule to a cultured mammalian cell, does not reasonably provide enablement for delivery to a non-mammalian cell in culture or any animal cell *in vivo*. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Claims 42-44 and 47 remain rejected under 35 U.S.C. 112, first paragraph, for the reasons of record set forth in the Office action of 16 Sep. 2002, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Applicant's arguments filed 17 Mar 2003 have been fully considered but they are not persuasive.

With respect to claim 41, Applicant merely asserts that the amendment to claim 41 overcomes the rejection, without explaining how. Claims 41-44 and 47 have all been amended to limit the methods to being practiced on mammalian cells or on mammals. Consequently, the issue of the scope of the target cell or animal has been overcome.

Claim 41 still embraces mammalian target cells *in vivo*, and the remaining grounds of rejection of claims 41-44 and 47 concerns whether the original specification enables how to use the claimed methods for delivering DNA molecules, using the recited adenoviral vectors, to mammals. Applicant's arguments simply repeat the contents of the declaration filed 3/18/03 under 37 CFR 1.132.

The declaration under 37 CFR 1.132 filed 18 Mar. 2003 is insufficient to overcome the rejection of claims 41-44 and 47 based upon lack of enablement as set forth in the last Office action. Pages 1-2 of the declaration describe experiments carried out after the filing of the application, and describe new adenoviral vectors based upon OAV287 that are not disclosed in the original specification. First of all, this information was not presented in the original application and thus cannot support enablement of the claimed invention, since the enablement requirement must be met at the time the invention was made. Second, it is not clear how this information relates to using the originally adenoviral vectors to deliver DNA molecules to mammals.

Pages 2-4 of the declaration describe experiments using OAV205 to deliver DNA encoding the 45W antigen of *Taenia ovis* to sheep as a vaccine. The results showed that administration of OAV205 resulted in a low level production of IgG1 and IgG2 antibodies against the 45W antigen. However, the specification does not teach a use for the method that

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simply results in production of antibodies against the non-adenoviral protein encoded by the vector. Rather, in this context the specification teaches to use the method for vaccination, i.e. inducing a protective immune response. The declaration shows that while OAV205 could be used effectively as a primer or booster to produce a protective immune response in conjunction with 45W protein or as a booster with a plasmid-based vaccine, it does not show that OAV205 used alone would produce a protective immune response. It also fails to show if even this limited use of the claimed method as part of a vaccination method would extend to antigens of other pathogens. The instant specification does not teach using the claimed adenovirus simply as part of a vaccination scheme involving other vaccine preparations, e.g. the protein itself or a plasmid-based vaccine.

In addition, according to the specification the claimed methods also embrace using the adenoviral vectors in gene therapy or genetic engineering to promoter growth or modify production traits. Nothing in the declaration addresses these uses, which are very different than use as a vaccine vector, i.e. the showing in the declaration is not commensurate in scope with the claims.

Claims 27, 29 and 47 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 27 recites the limitations "the sequence" and "the amino acid sequences" in lines 3-4. There is insufficient antecedent basis for these limitations in the claim. This would be overcome by replacing "comprises at least one nucleotide difference ... encoded thereby" with --

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is identical to nucleotides 1-29,574 of SEQ ID NO: 3 except for differences in nucleotide sequences encoding viral polypeptides that do not alter the amino acid sequences encoded by SEQ ID NO: 3--.

Claim 29 recites the limitation "the nonessential portion" in line 6. There is insufficient antecedent basis for this limitation in the claim.

Claim 47 recites "wherein adenovirus vector infects" in line 7. It is unclear what connection this limitation has to do with the method step of administering "an adenoviral vector." This ambiguity would be corrected by replacing "adenovirus vector" with -- the adenoviral vector --.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

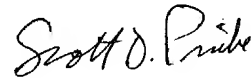
A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Scott D. Priebe whose telephone number is (571) 272-0733. The examiner can normally be reached on M-F, 8:00-4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy J. Nelson can be reached on (571) 272-0804. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Scott D. Priebe
Primary Examiner
Art Unit 1632